RENAL FUNCTION IMPAIRMENT AND ASSOCIATED FACTORS AMONG ADULT HIV POSITIVE PATIENTS ATTENDING ANTIRETROVIRALTHERAPY CLINIC IN METTU KARL REFERRAL HOSPITAL

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A THESIS REPORT SUBMITTED TO DEPARTMENT OF EPIDEMIOLOGY, FACULTY OF PUBLIC HEALTH, INSTITUTE OF HEALTH, JIMMA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTERS OF PUBLIC HEALTH IN EPIDEMIOLOGY

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Abstract

Background: Renal function impairment is defined as the occurrence of elevated levels of protein or albumin in the urine or an elevation in serum creatinine. It is associated with an increasing cause of morbidity and mortality in HIV positive individuals than in the general population. Identification of factors associated with renal function impairment is important in order to institute appropriate interventions for the purpose of renal function status.

Objective: The main aim of this study is to assess the magnitude of renal function impairment and its associated factors among adult HIV positive attending ART clinic in Mettu Karl Referral Hospital, Mettu town, Southwest Ethiopia, 2020.

Methods: Methods: An institution-based cross-sectional study was conducted from March 8-May 20, 2020. Systematic sampling technique was employed to select 359 study participants. Data was collected by face to face interview using pretested structured questionnaire. Serum creatinine was calculated as an estimate of renal function (eGFR) using chronic kidney disease epidemiological collaboration equation. Weight and height was measured using portable Seca digital floor and Seca measuring rod respectively. Descriptive statistics was used to describe the data depending on its nature. Bivariable and multivariable logistic regression analyses were used and variables with P≤ 0.25 in bivariable analysis were entered into the multivariable logistic regression. Adjusted Odds ratio (AOR) with 95 % Confidence interval was estimated to identify the predictors of renal function impairment. The statistical significance was declared at p-value of less than 0.05. The finding of the study was displayed by using tables and graphs.

Result: A total of three hundred and fifty two HIV infected patients participated in this study with response rate of 98.1%. Out of 352 HIV patients on ART, 73 (20.7%) were found to have renal function impairment. Smoking cigarette [AOR= 8.48, 95% CI: 4.60-15.64], Diabetes mellitus [AOR= 4.29, 95% CI: 2.28-8.09], Hypertension [AOR= 2.13, 95% CI: 1.06-4.29] and low CD4 count [AOR=4.31, 95% CI: 2.49-7.44] were found to be independent predictors of renal function impairment among adult HIV positive patients.

Conclusion: The prevalence of renal function impairment among HIV patients on ART is high. Hypertension, diabetes, Smoking cigarette and low CD4 count were associated factors of renal function impairment.

Keywords: Renal function impairment, HIV Positive, ART, Mettu

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Abbreviations and Acronyms

AIDS	Acquired Immune Deficiency Syndrome
AKI	Acute Kidney Injury
ART	Antiretroviral Therapy
ARV	Antiretroviral
BMI	Body Mass Index
CD4	Cluster of Differentiation 4
CG	Cockcroft Gault
CKD	Chronic Kidney Disease
CKD EPI	Chronic kidney disease epidemiology collaboration
CrCl	Creatinine Clearance
DART	Development of Antiretroviral Therapy in Africa Trial
eGFR	estimated Glomerular Filtration Rate
ESRD	End Stage Renal Disease
GFR	Glomerular Filtration Rate
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
HIVAN	Human Immune Deficiency Virus Associated Nephropathy
KDOQI	Kidney Disease Outcome Quality Initiative
MDRD	Modification of Diet Renal Disease
TDF	Tenofovir Disoproxil fumarate
WHO	World Health Organization

Chapter 1: Introduction

1.1 Background

Renal impairment is defined as the two primary laboratory indicators of kidney abnormalities that include the occurrence of elevated levels of protein or albumin in the urine (proteinuria and albuminuria) or an elevation in serum creatinine (1). The National Kidney Foundation clinical practice guideline classified renal impairment based on the glomerular filtration rate (GFR) by using Cockcroft-Gault technique. Thus, accordingly, an estimated GFR value of ≥90ml/min/1.73m^2 is normal, 60-89ml/min/1.73m^2 is mild, 30-59ml/min/1.73m^2 is moderate, 15-29ml/min/1.73m^2 is severe and <15ml/min/1.73m^2 is kidney failure. Based on the classification renal function impairment is defined as eGFR<60ml/min/1.73m^2 (2).

Human Immunodeficiency virus (HIV), is a virus that affects every organ system in the body through impairment or by rendering the host vulnerability to opportunistic infections (3). Kidney is an essential organ in human body system and it plays the vital organ in the excretion of waste products and toxins (urea, creatinine and uric acid), regulation of extracellular fluid volume, serum osmolality and electrolyte concentrations (4).

Despite this fact, kidney is among the commonest sites of infection in HIV positive patients (3). Renal disease in HIV-infected persons manifests in a multiple of ways, including acute kidney injury (AKI), HIV-associated kidney disease, comorbid chronic kidney disease (CKD), and treatment-related kidney toxicity (5). Screening for renal disease is usually recommended for all HIV-infected persons at diagnosis of the infection and at the beginning of antiretroviral therapy (ART) (6).

The etiologies of renal impairment in HIV positive individuals are multiples. These are; exposure to HIV viremia, chronic systemic inflammation, and potentially nephrotoxic ART drugs and co-medications, in addition to cardiovascular disease (CVD) and renal risk factors such as hypertension, diabetes, and smoking, which may affect glomerular, tubulo -interstitial, and Reno-vascular integrity (7).

If not detected and managed timely and properly, Acquired Immune Deficiency Syndrome (AIDS)-associated renal disease might progress to an end-stage renal disease (ESRD) requiring renal replacement therapy (8). HIV associated nephropathy is a fourth leading disorder

contributing to death among those that have progressed to AIDS patients proceeding sepsis, pneumonia, and liver disease (9). Despite high magnitude of renal impairment in HIV positive, early diagnosis and regular monitoring for renal impairment is essential on behalf of prognosis, medication dosing and treatment (10). Identification of factors associated with renal function impairment is important in order to institute appropriate interventions for the purpose of renal function status.

1.2. Statement of the problem

Renal function impairment is a global public health problem; moving from 27th to the18th most important worldwide cause of death within the last two decades, this degree of shift was the second only to HIV/AIDS (1). Globally, renal function impairment among adults living with HIV estimated using the modification of diet renal disease (MDRD) was 6.4%, whereas 4.8% and 12.3% by using the Chronic kidney disease epidemiology collaboration (CKD-EPI) equation and the Cockcroft gault (CG), respectively. Renal function impairment is different in various part of the world; its magnitude in North America was found to be 6.5%, in South America 6.2%, in Europe 2.7% (11). In sub-Saharan Africa (SSA) the prevalence of renal function impairment in people living with HIV (PLWHIV) has been shown to be high ranging from 25% to 77% (12–14). In Ethiopia, studies conducted in Bahir Dar town and Jimma showed that 30.1% and 18.2% of patients had renal function impairment, respectively (15,16).

The risk of kidney disease remains greater in HIV infected individuals than in the general population and it was associated with poor outcomes, including increased morbidity and the risk of death. For instance there is an evidence that indicated 15% increased prevalence of renal impairment per year of additional exposure to antiretroviral (ARV) (17). World Health Organization recommends assessing creatinine clearance for patients at initiation of tenofovir and every 6 months ‘if feasible’, although inability to test does not preclude tenofovir use (18).

The study conducted in a review article in South Africa found that HIV RNA levels >4,000 copies/ml, low CD4 counts, personal history of kidney disease and hepatitis C co-infection were associated with a high risk of rising renal function impairment in HIV infected individuals (19).

Some study showed that ART associated renal function impairment was associated with causal risk factors such as administration of other renal toxic drugs, female gender, longer period on ART, dehydration, opportunistic infections (15,20–22).

Separately from traditional possible factors for renal function impairment such as aging, hypertension and diabetes, the increased-risk for renal function impairment in PLHIV might be described by HIV and ART-related factors (23–25). Decreased GFR, elevated serum creatinine level and high level of protein in urine sample are common among HIV positive individuals (8).

Renal function impairment that might progress to end-stage renal disease requiring dialysis and renal transplant can be diagnosed in its earlier stage through routine screening and careful attention to changes in renal functions (26). However, in developing countries like Ethiopia where renal transplant and dialysis services are rarely accessible, early detection of renal disease have some clinical and financial implications for people living with HIV/AIDS (27). Though, the guide line recommend basic chemistry test every 3-6 months (28). regular laboratory monitoring may not be necessary for making sound antiretroviral (ARV) treatment decisions in resource-limited settings (29), the risk of undiagnosed HIV associated renal impairments is worrisome in these settings where routine laboratory testing is often not available (12).

Renal impairment at the time of initiation of ART or during ART is associated with complications such as faster progression to AIDS , bone demineralization and anemia which present significant challenges to HIV management especially in resource limited settings or no access to renal replacement therapy (RRT) (30).

Renal function impairment is a world health burden with a high economic cost to health systems(31). The average cost of hospitalization for patients with renal function impairment is also significantly higher compared to non-renal function impairment (32). High-income countries typically spend more than 2-3% of their annual health-care budget on the treatment of end-stage kidney disease, although those receiving such treatment represent lower than 0.03% of the total population (33). In 2010, 2.62 million people received dialysis global and the prerequisite for dialysis is projected to be double by 2030 (1). The costs involved in the management of renal function impairment with co-morbidities are very high, imposing great difficulties on health care systems, predominantly in countries with limited resources (34).

Quality of life will be reduced progressively in the renal function impairment (35). Patients with renal disease have a decreased quality of life and an increased frequency and severity of both symptoms and psychological distress, with the magnitude of these changes negatively correlated with GFR (36).

Recognition of common risk factors for kidney disease in HIV infected patients is important to guide efforts aimed at prevention and early diagnosis. Despite this fact, data regarding renal impairment in HIV disease among Ethiopians is rare.

In the existence of limited previous literature, few studies in other countries have included behavioral variable like smoking cigarette as a factor predicting renal function impairment among adult living with HIV on ART but no study have considered behavioral variable from the few studies in Ethiopia. So, this study will try to incorporate all substantial factors that can influence renal impairment in HIV positive patients. Furthermore, despite the study area is found in the high magnitude areas for HIV/AIDS risk priority (37), there is no study attempted concerning renal impairment in the specified study area.

Also the Guideline and study recommend the use of CKD EPI equation to calculate eGFR in HIV infected patients compared to other equation (38,39) but no study considered CKD EPI from the few studies in Ethiopia. Therefore, the aim of this study is to assess the prevalence of renal function impairment by CKD EPI equation and associated factors among adult HIV positive patients attending ART clinic in mettu Karl referral hospital.

Chapter 2: Literature review

2.1 Prevalence of renal function impairment with HIV/AIDS

Several studies conducted in different parts of the globe indicate that renal function impairment is a common comorbidity among HIV positive individuals. A cross-sectional study in the Multicenter AIDS Cohort Study conducted in US urban areas (2011) on chronic kidney disease and estimates of kidney function in HIV infection found renal function impairment was 7% among HIV infected patients (40). Similarly, the systematic review and meta-analysis done in North America in the year 2018 among HIV positive adults showed that renal function impairment was 7% (11). A cross-sectional study done in brazil (2011), on the prevalence and risk factors associated to chronic kidney disease in HIV-Infected patients on HAART and undetectable Viral Load also showed that 8.4% had renal function impairment (17).

A cross sectional study (2011) on clinical characteristics of kidney disease in Japanese HIV-infected patients indicated 15.4% of renal function impairment (41).However, in china (2015) nationwide retrospective cohort conducted on renal function in HIV-Positive individuals following initiation of Antiretroviral Therapy showed that the prevalence renal function impairment was 1.7% (42).

In Europe, finding from a retrospective, cross-sectional study conducted in northern Italy (2013) on prevalence of renal disease within an urban HIV-infected adults showed that prevalence of renal impairment was 27% (43). On contrary to this study, findings from a retrospective analysis of a clinical database collected between January 2000 and February 2014 on adults living with HIV/AIDs in Italy indicated 11.9% of renal function impairment (44). A cross-sectional study conducted in Spain (2014) on prevalence and associated factors of abnormal renal function in HIV-infected patients showed 2.8% of renal function impairment (45).

In African countries, the existence of renal function impairment in HIV/AIDS patients is becoming a major public health problem. A cross-sectional study conducted at University of Benin teaching hospital in Nigeria (2011) indicated that the prevalence of renal function impairment was 53.3% (46). A cross-sectional survey conducted in adults living with HIV follow up in 4 outpatient HIV-clinics in Bujumbura, Burundi in February 2008-2009 revealed 45.7% renal function impairment (24). On contrary to these study, a retrospective study

conducted among HIV-1 infected patients attending the antiretroviral clinic at the Jos university teaching hospital in Nigeria (2011) showed 23.8% renal function impairment (47). A cross-sectional study conducted in south-west Nigeria (2012) on prevalence of chronic kidney disease in HIV positive adult patients reported that 23.5% had renal function impairment (48). Similarly a cross-sectional study conducted at UNTH Ituku Ozalla, referral hospital in south-south states of Nigeria (2014) showed that the prevalence of renal function impairment was (24.3%) (49). Furthermore, in the 2015 study conducted in the north central Nigeria University of Ilorin teaching hospital, Kwara state a tertiary health institution providing tertiary health care services showed that the prevalence of renal function impairment was 24% (50).A Cross-sectional study carried out in the outpatient HIV clinic at Bugando medical Centre in Mwanza, Tanzania from November 2009 and February 2010 showed that 24.5% developed renal function impairment(26).

Findings from a retrospective analysis of a clinical database collected from May 2010 to January 2011 on prevalence of renal dysfunction and association with risk of death amongst HIV-infected in Komfo Anokye teaching hospital (KATH) in Kumasi, Ghana indicated 38.8% of renal function impairment (13). But, another cross-sectional study carried out at the antiretroviral (ART) clinic in Bolgatanga hospital, East Ghana (2013) on renal insufficiency in Ghanaian HIV infected patients revealed a 14.5% prevalence of renal function impairment (51).

A cross-sectional study conducted in adults living with HIV/AIDS on renal function impairment and associated risk Factors at Felege Hiwot referral hospital, Northwest Ethiopia (2013) showed that 30.1% of the patients developed renal function impairment (15). However, a cross sectional study conducted at comprehensive and chronic care center of the Jimma University Specialized Hospital (JUSH) in Jimma Town, Southwest Ethiopia (2016) on renal function impairment and associated factors among HAART Naïve and experienced adult HIV Positive showed a lower prevalence of renal impairment, 18.2% of patients with HIV had renal function impairment (16).

2.2 Factors associated with renal function impairment in Adults Living with HIV.

2.2.1. Socio-demographic factors

Evidences showed that age of an individual was an independent predictor for renal function impairment, the older the age the greater the risk. A cross-sectional study done in 2011 in Japan adults living with HIV/AIDs showed that older age (≥ 52) had significantly associated with renal function impairment (41). Also a cross-sectional study conducted on prevalence of renal dysfunction and association with risk of adults amongst HIV-infected in Kumasi, Ghana (2013) showed the same finding, older age (≥40 age) had significantly associated with renal function impairment (13). Further, a cross- sectional study conducted in southwest Ethiopia (2016) on renal function impairment and associated factors among HAART naïve and experienced adult HIV positive individuals showed that older age (≥50) had significantly associated with renal function impairment (16).

Sex is also one of an important factor associated with renal function impairment, being female increases the risk. A cross-sectional study done in Mwanza, Tanzania (2011) on renal dysfunction among HIV-infected starting antiretroviral therapy showed being Female is significantly associated with renal function impairment (12). Similarly a cross-sectional study done in southwest Ethiopian (2016) on renal function impairment and associated factors among HAART naïve and experienced adult HIV positive individuals showed being Female is significantly associated with renal function impairment (16).

A cross-sectional study conducted in Gulu hospital, Northern Uganda (2015) on impaired renal function and associated risk factors in newly diagnosed HIV-infected adults showed that there is no statistically significant association between occupation and renal function impairment (20).

A cross-sectional study conducted in Gulu hospital, Northern Uganda (2015) on impaired renal function and associated risk factors in newly diagnosed HIV-infected adults showed that there is no statistically significant association between residence and renal function impairment (20). Also, a cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that there is no statistically significant association between residence and renal function impairment (15).

A cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that there no statistically significant association between educational status and renal function impairment (15).

A case-control study conducted in South Africa (2011) on kidney function and the risk of cardiovascular events in HIV-1 infected patients showed that there is no statistically significant association between family histories of renal disease and renal function impairment (52).

A cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that there is no statistically significant association between marital status and renal function impairment (15).

A cross-sectional study conducted in Gulu hospital, Northern Uganda (2015) on impaired renal function and associated risk factors in newly diagnosed HIV-infected adults showed that there is no statistically significant association between income and renal function impairment (20).

2.2.2. Behavioral factors

A study conducted in France (2000) on effects of current smoking and smoking discontinuation on renal function and proteinuria showed that cigarette smokers had significantly associated with renal function impairment (20). But, a cross-sectional study conducted in Gulu hospital, Northern Uganda (2015) on impaired renal function and associated risk factors in newly diagnosed HIV-infected adults showed that there is no significance associated between cigarette smoking and renal function impairment (20).

2.2.3. Bio-clinical factors (HIV related).

Different studies stated that the presence of comorbidities such as hypertension and diabetes were among factors associated with renal function impairment among patients with HIV. A cross-sectional study conducted in Porto Alegre, Brazil (2011) on prevalence and associated factors with chronic kidney disease (CKD) in a cohort of HIV positive individuals with undetectable viral load on HAART indicated that hypertensive patients had significantly associated with renal function impairment (17). Similarly a cross-sectional screening conducted in Kinshasa, Congo, (2012) on prevalence of low estimated glomerular filtration rate, proteinuria, and associated risk factors among HIV-infected black patients using Cockcroft-Gault and modification of diet in renal disease study equations showed that patient with hypertension

had significantly associated with renal function impairment (53). Further, a cross sectional study conducted in university of Mississippi health care, USA (2010) on screening for chronic kidney disease in the ambulatory HIV population indicted patients with Diabetes mellitus had significantly associated with renal function impairment (54).

Available evidences also identified an individual's body mass index as a statistically significant factor associated with renal function impairment. A cross-sectional study conducted in Barcelona, Spain (2014) on high prevalence of signs of renal damage despite normal renal function and associated factors in a HIV-infected patients showed that patients with body mass index <18.5 or >30kg/m2 had significantly associated with renal function impairment (45). Also, a cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that patients with low body mass index (<18.5) had significantly associated with renal function impairment (15).

Furthermore, clinical stage of HIV infection was identified as determinant for renal function impairment. A cross-sectional study done in Mwanza, Tanzania (2011) on renal dysfunction among HIV-infected starting antiretroviral therapy showed that patients with advanced WHO stage (stage 3 and 4) had significantly associated with renal function impairment (12).Similarly a cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that patients at advanced WHO had significantly associated with renal function impairment (15).

CD4 count was also another pertinent factor associated with renal function impairment among HIV positive adults, the lower the CD4 count the higher risk for renal function impairment. A cross-sectional study conducted in Gulu hospital, north Uganda (2015) on impaired renal function and associated risk factors in newly diagnosed HIV-infected adults showed that patients who had CD4 cell count < 350 had significantly associated with renal function impairment (20). Similarly a cross-sectional study conducted in northwest Ethiopia (2013) on renal function impairment and associated risk factors among HIV positive individuals showed that patients who had CD4 cell count < 200 had significantly associated with renal function impairment (15). Also, a study conducted in Addis Ababa (2019) on reduced kidney function in tenofovir disoproxil fumarate based regimen and associated factors showed that patients with CD4 cell count < 200 had significantly associated with renal function impairment (55).

Moreover, presence of opportunistic infection determines the risk for renal function impairment. A cross-sectional survey conducted in Burundi (2011) on prevalence of chronic kidney disease among people living with HIV/AIDS indicated that patients with history of opportunistic infection had significantly associated with renal function impairment (24).

A cross-sectional survey conducted in Vietnam (2013) on WHO antiretroviral therapy guidelines 2010 and impact of Tenofovir on chronic kidney disease in Vietnamese HIV-infected patients indicated that patients who use tenofovir had significantly associated with renal function impairment (56).

Generally, regardless of substantial improvement, HIV remains a heavy health risks for adults and renal function impairment increases these risks. So, in the area where there is a paucity of study in this population, understanding the experience of renal function impairment and its determining factors will play an important role in curbing of this epidemic for adults through detection and treatment of the disease.

2.3. Conceptual framework

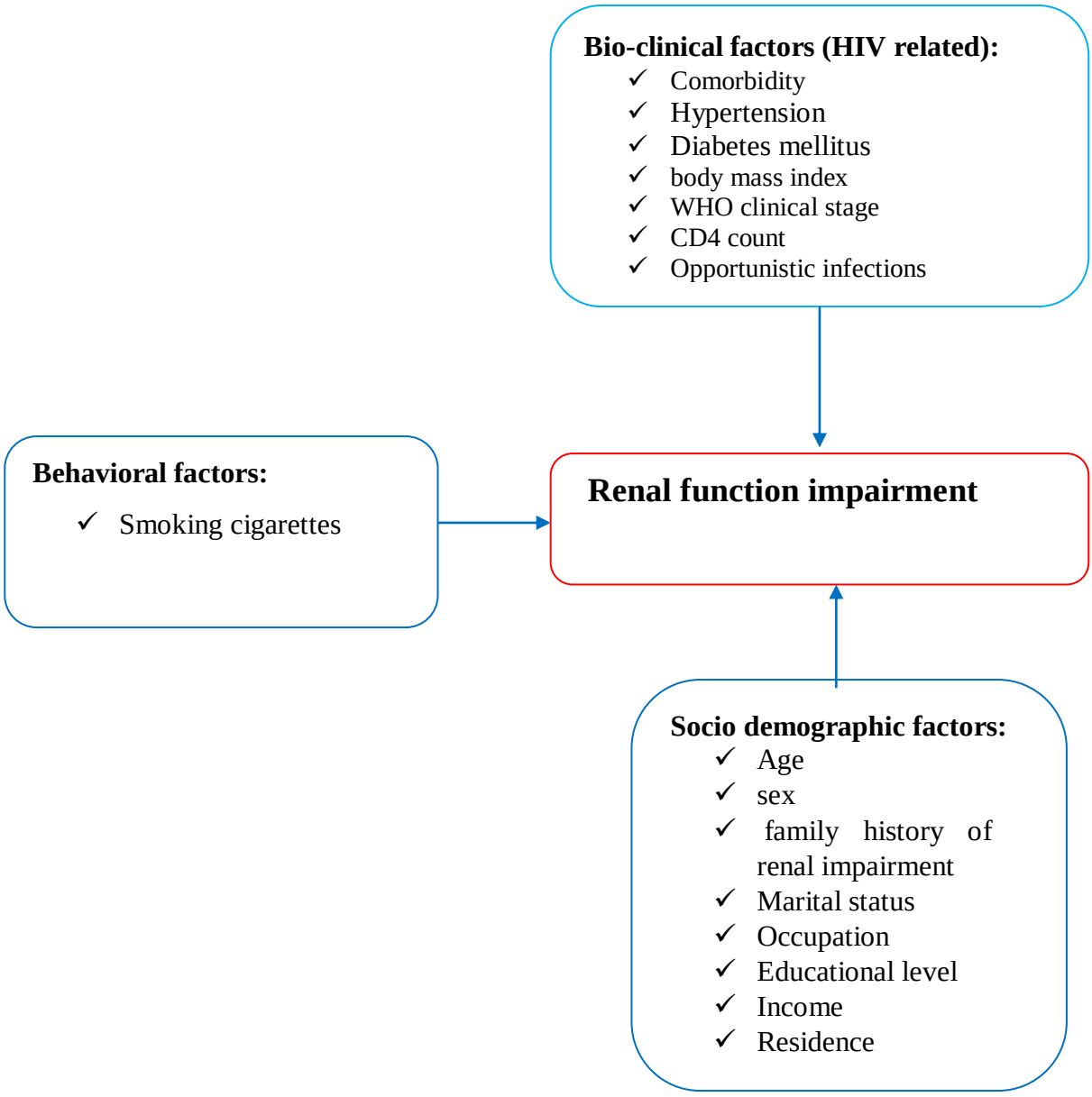

Figure 1: Conceptual framework for factors associated with renal function impairment of adults living with HIV/AIDS attending ART clinic at Mettu Karl Referral hospital. Developed by reviewing different literatures (15,16,20,57–59)

2.4. Significance of the study

The result of this study will enhance the existing limited body of knowledge regarding the prevalence of renal function impairment and associated factors among HIV positive patients and also assist as a basis for future renal function problem investigation in this range through increasing concern of the problem in Ethiopia. Identification of asymptomatic patients will aid in early management of patients. Early diagnosis and regular monitoring for renal function impairment is essential on behalf of prognosis, medication dosing, and treatment. It will also serve as a clinical reference to HIV care and treatment providers who may use the findings to offer all-inclusive services to adults living with HIV. The finding of this study will similarly help in the persuasion of designing suitable policy, plan and intervention programs aimed at renal function impairment management in HIV/AIDS care settings. Furthermore, the study will be used as an input for studies targeting the problem.

Chapter 3: Objectives

3.1. General objective

To assess the magnitude of renal function impairment and its associated factors among HIV positive adult attending ART clinic in Mettu Karl Referral Hospital, Mettu town, Southwest Ethiopia, 2020.

3.2. Specific objectives

To determine the prevalence of renal function impairment among HIV positive adult attending ART clinic in Mettu Karl Referral Hospital, Mettu town, Southwest Ethiopia, 2020.

To identify factors associated with renal function impairment among HIV positive adult attending ART clinic in Mettu Karl Referral Hospital, Mettu town, Southwest Ethiopia, 2020.

Chapter 4: Methods and materials

4.1. Study area and period

The study was conducted at Mettu Karl Referral Hospital in Mettu town, southwest Ethiopia from March 8-May 30, 2020. Mettu town is located 600 km in the southwest direction of Addis Ababa, the capital city of Ethiopia. Total population of the town is 50,521 from which 26,534 are females. Mettu Karl Referral Hospital is one of the public health facilities that are currently providing HIV/AIDS care and treatment. It is providing services for the catchment population of about 1.3 million people. The hospital has 214 beds and 145 health supporters & 171 health professionals including internist, general surgeon, emergency surgery, gynecologist, general practitioners and others. Currently, the total numbers of patients who are attending ART clinic are1, 600 of which 1,378 are Adults.

4.2. Study design

An institution based cross-sectional study design was employed.

4.3. Population

4.3.1. Source population

All HIV infected Adults (age >18 years old) on ART at Mettu Karl Referral Hospital ART clinic.

4.3.2. Study population

Selected HIV positive adults on ART, who have a follow up in Mettu Karl Referral hospital ART clinic during the study period, and who fulfilled the eligibility criteria.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

HIV positive adults aged above 18 years

Being on ART for 6 months and above

4.4.2. Exclusion Criteria

Those who were seriously ill unable to communicate and pregnant women

4.5. Sample size calculation and Sampling technique

4.5.1 Sample size calculation

Sample size was calculated for both objectives separately by using STATCALC of Epi info for different variables and the highest sample size was used as shown in the following table.

Table 1 Sample size determination for renal function impairment among HIV patients attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest, Ethiopia, 2020

Sample size for first objective								
Variable	Proportion	Confidence level	Margin of error	Total population	Sample size	5% Non-response rate	Final sample size	Ref.
Renal function impairment in HIV positive adult	25.4%	95%	4%	1378	342	17	**359**	(55)

Sample size for the second objectives									
Variables	% of outcome among unexposed	% of outcome among exposed	OR	Confidence level	Ratio	Power	5% non-respondent rate	Final sample size	Reference
Age ≥50	24.1	48.4	2.9	95%	1:1	80	7	145	(16)
Advanced WHO stage	23.3	47.1	2.9	95%	1:1	80	7	149	(16)
CD4count <200	73.9	26.1	0.1	95%	1:1	80	2	42	(16)
low BMI	68.6	24.2	0.1	95%	1:1	80	2	48	(15)

4.5.2 Sampling technique

The representative sample was selected using a systematic random sampling technique. The individual patients were approached through calculating sampling interval K^{th}, [N/n]. Accordingly, the total number of Adults Living with HIV/AIDS (N= 1378), of whom (n= 359) are the calculated final sample size that yields a sampling interval of three. The first patient to be interviewed was selected using the lottery method from the first three individuals. Finally, study participants were, picked every third patient that came to the ART clinic during the study period to make the exit interview.

4.6. Data collection procedures (instrument, personnel, technique)

4.6.1 Data collection instruments

Data was collected using pretested structured questionnaire in order to capture information on socio-demographic characteristics, behavioral factors and bio-clinical (HIV-related) factors. Checklist was used to collect data from medical record for the outcome variable. The serum creatinine was calculated as an estimate of renal function (eGFR) using chronic kidney disease epidemiological collaboration (CKD-EPI) equation. Renal function impairment was defined as eGFR < 60ml/m/1.73m^2 (10).

eGFR Measurement equation:

For female with serum creatinine ≤ 0.7mg/dl: $GFR = 166 \times (Scr/0.7)^{-0.329} \times (0.993)^{Age}$

Female with serum creatinine > 0.7mg/dl: $GFR = 166 \times (Scr/0.7)^{-1.209} \times (0.993)^{Age}$

For male with serum creatinine ≤ 0.9mg/dl: $GFR = 163 \times (Scr/0.9)^{-0.411} \times (0.993)^{Age}$

Male with serum creatinine > 0.9mg/dl: $GFR = 163 \times (Scr/0.9)^{-1.209} \times (0.993)^{Age}$ (57).

Here, age is in year and serum creatinine is in mg/dl.

Anthropometric measurement

Participants' weight was measured by portable Seca digital floor weight scale. The scale was calibrated regularly to ensure accurate measurements. Participants were informed to wear minimum clothing and standing upright and unsupported in the middle of the scale's platform. Reading of weight was taken to the nearest 0.1g. Participants' height was measured using Seca

measuring rod. Participants were informed to be barefoot, legs straight, shoulders relaxed and to look straight ahead at the horizontal plane. With each participant looking straight ahead along the Frankfort plane, the headpiece was lowered to touch the crown of their head gently but firmly. Reading of height measurement was taken to the nearest 0.1cm. Then, BMI of the participants was calculated as weight in kg divided by height in meters squared and subjects were considered as underweight (BMI<18.5 kg/m^2) , normal (BMI= 18.5- 24.9 kg/m^2) and overweight (BMI ≥ 25 kg/m^2) (15)

Blood Sample Collection and Handling

Blood specimens were collected from each study participant for laboratory investigations. Five ml of venous blood was drawn from each participant into a syringe for renal function test. The blood sample was dispensed into jell coated serum separator test tube and centrifuged at 3500 revolution per minute for 10 minutes for the separation of the serum. Serum was frozen at (-18˚C) when analyses are not carried out immediately. Serum creatinine was estimated using Roche/Hitachi 902 Analyzer, Germany.

4.6.2. Data collection personnel

Data was collected by two trained Bachelor Degree holder Nurses, Bachelor Degree holder Laboratory technologist draw the blood sample and one medical doctor supervisor regulated and managed the data collection procedure.

4.6.3. Data collection technique

Data was collected using face-to-face structured questionnaire. Medical record of adults living with HIV/AIDS was reviewed to extract data on CD4, WHO stage, current drug regimen, opportunistic infection, comorbidity, hypertension, diabetes, regular follow-up.

4.7. Study Variables

4.7.1. Dependent variable

Renal function impairment

4.7.2. Independent variables

Socio-demographic variables: Age, Sex, Residence, Educational level, Occupation, Marital status, income, family history of renal disease.

Behavioral factors: cigarette smoking

Bio-medical (HIV-related) variables: opportunistic infections, Comorbidity (diabetes, hypertension), Tenofivir-based regimen, CD4 counts, body mass index, WHO stage.

4.8. Operational definition

Renal impairment: defined as eGFR < 60ml/min/1.73m^2 calculated by the CKD EPI equation.

WHO stage: Stage 1, stage 2, stage 3 and stage 4 according to WHO (60).

Adult: an individual whose age was greater than 18 years old.

Current Smoking: at least one cigarette per day in the past 30 day.

Opportunistic infection: an individual who had other communicable disease/s.

Co morbidity: an individual who had other chronic non-communicable disease/s.

4.9. Data processing and analysis

Data were manually checked for completeness and coded, cleaned before entering to a computer. Then, it was entered into Epi Data version 3.1 and exported into SPSS version 22 for analysis. Data exploration was conducted to assess the completeness and descriptive statistics was used to describe the data. Bivariable analysis was employed to determine presence of association between renal function impairment and each independent variable. Variables that were found significant at p-value less than or equal to 0.25 in bivariable analysis were selected as candidate variables for multivariable logistic regression analysis. Multi-collinearity was done by checking variance inflation factor (VIF) less than 10 percent and there were no problems with multi-collinearity identified (VIF < 10%). Multivariable analysis was carried out to identify independent predictors of renal function impairment by controlling for confounders. Backward stepwise logistic regression variable selection method was used P-value less than 0.05; AOR with their respective 95% of CI was used to identify independent predictors for renal function impairment. The model fitness was tested by using Hosmer and Lamshow goodness of fit test and the model was declared fit (P=0.250). Finally, the results were presented by using tables, graphs and narration.

4.10. Data quality management

Data quality was controlled by adopting validated tools via reviewing literatures, giving training to data collectors and supervisors, conducting pretest, and language translation. Accordingly, one-day training was given to the data collectors and supervisors prior to data collection by the

principal investigator on the objective of the study, method of data collection. A pretest on 5% of the sample size in Bedele general hospital to check the clarity and consistency of the questionnaire and the checklist was done prior to the actual data collection. Relevant modifications was made as per required. Questionnaire was primarily prepared in the English language and was translated into Afaan Oromo language by professional who is familiar on this field and fluent in the two languages and back-translated to English language by another expert, who was not familiar with the original questionnaires in order to guarantee its consistency.

During the data collection time, each completed questionnaire was checked for completeness, clarity, and consistency at the site of data collection by the supervisors to take the corrective measure on daily basis. The overall activities were also monitored by the principal investigator.

After data collection was completed, collected data was entered using Epi data software. After data entry, cleaning was done using Statistical Package for Social Science (SPSS) and crosstab was done to check the apportionment size of the independent variables with the dependent variable to check for the assumptions.

Moreover, for better quality of the laboratory result, blood specimen was collected, processed and analyzed following standard operating procedures (SOP). The result of laboratory test was recorded on the standardized report format carefully and attached to questionnaire according to subject's unique identification number. Carefully and attached to questionnaire according to subject's unique identification number.

4.11. Ethical consideration

Ethical clearance and approval letter were obtained from institutional review board of Jimma University, institute of health. An official letter of support was secured from Mettu Karl referral Hospital. Informed written consent was obtained from each participant after describing the benefits and risks of the study. Anonymity was kept; during specimen collection and interview. Any information concerning the participants was kept confidential and the specimens collected from the participants were analyzed only for the intended purposes. Result where eGFR< 60ml/min per $1.73m^2$ was communicated to internal medicine unit in the hospital for appropriate management.

4.13. Dissemination of the result

Final result will be submitted to Jimma University, Institute of Health, Public Health Faculty, and Department of Epidemiology. In addition, Mettu Karl Referral Hospital office will be provided with the final report. Efforts will be made to publish the finding on reputable peer reviewed scientific journal.

5. RESULTS

5.1. Socio-demographic Characteristics

A total of three hundred and fifty two HIV infected patients participated in this study with response rate of 98.1%. Out of total participants, 198 (56.2%) were females. The mean (±SD) age of the study participants was 43.42 (± 13.95) years. Majority, 172 (48.9%) of the participants were Muslim followed by Orthodox 112 (31.8%) and. Out of the total, 207 (58.8 %) of them were married, 161(45.7%) completed Diploma and above, 185(52.6%) were government employee, 274 (77.8%) were from urban residents and 177(50.3%) had family monthly income of greater than 3500 birr (ETB) **(Table 2).**

Table 2: Socio-demographic characteristics of HIV patients on treatment attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest, Ethiopia, 2020

Characteristics	Categories	Frequency	Percentage (%)
Sex	Male	154	43.8
	Female	198	56.2
Age	<40	179	50.9
	≥40	173	49.1
Marital status	Single	70	19.9
	Married	207	58.8
	Divorced	75	21.3
Residence	Urban	274	77.8
	Rural	78	22.2
Religion	Orthodox	112	31.8
	Muslim	172	48.9
	Protestant	57	16.2
	Other	11	3.1
Educational	No formal educational	59	16.8
	Primary education	46	13.1
	Secondary education	86	24.4
	Diploma and above	161	45.7
Income	< 3500	175	49.7
	≥ 3500	177	50.3
Family history of renal impairment	No	323	91.8
	Yes	29	8.2

5.2. Behavioral Factors of participants

Among 352 Participants 60(17%) have history of smoking cigarette. Sixty (17%) are current smokers among this 55(91.7%) smoke every day and the rest 5(8.3%) smokes someday (Figure 2).

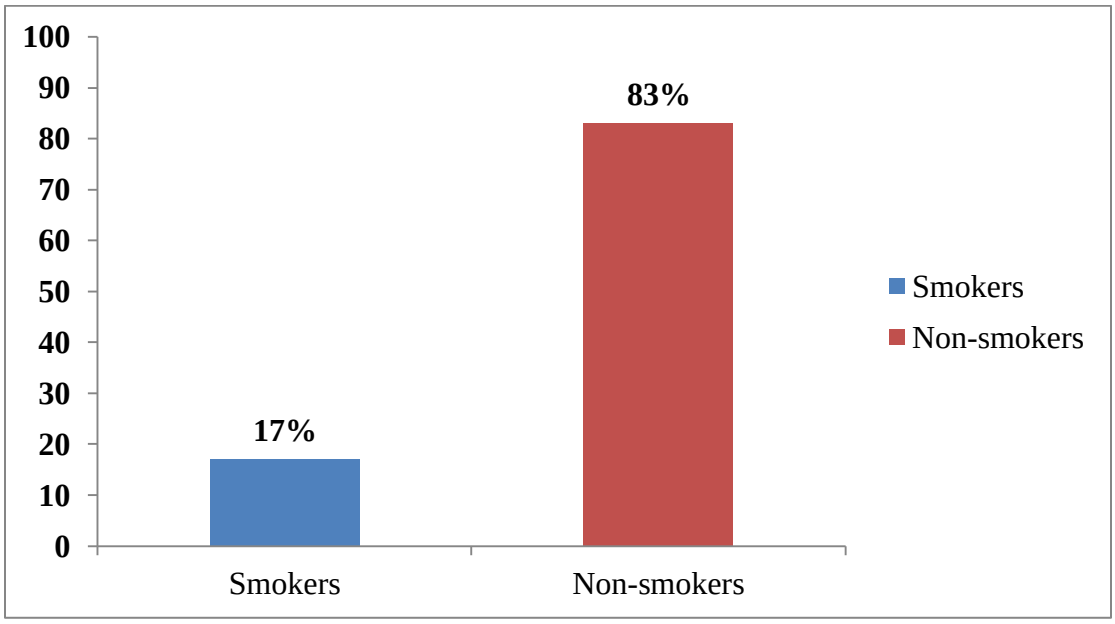

Figure 2: Behavioral factors of HIV patients on treatment attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest Ethiopia, 2020

5.3. Bio-clinical factors of the study participants

About 69 (19.6%) participants had opportunistic infections. Ninety six (27.3%) of the participants had comorbidity. Fifty (14.2%) of the participants were confirmed diabetic patients and on medication and 42 (11.9%) of respondents were confirmed hypertensive patients taking the medication. Twenty nine (8.2%) of participants had family history of renal disease.

About 333 (89.4%) of the participants on ART were receiving first line regimens and 252(71.6%) a combination of tenofovir (TDF). Two hundred thirty seven (67.3%) of the study participants were in advanced WHO clinical stage (Stage III & IV). Majority 225(63.9%) of the participants had a normal body mass index (BMI). The mean CD4 count was 251 ±107.9 cells\mm^3. One hundred thirty four (38.1%) of the participants on ART had CD4 count < 200 cells/mm^3. The mean (±SD) creatinine level was 0.99 (± 0.74) mg/dl. The mean (±SD) serum creatinine was 104.2 (±40.04) ml/min/1.73 m^2 **(Table 3)**.

Table 3: Bio-clinical factors of HIV patients on treatment attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest, Ethiopia, 2020.

Characteristics	Categories	Frequency	Percentage (%)
Comorbidity	No	256	72.7
	Yes	96	27.3
Opportunistic infections	No	283	80.4
	Yes	69	19.6
Diabetes mellitus	No	302	85.8
	Yes	50	14.2
Hypertension	No	310	88.1
	Yes	42	11.9
Body mass index	<18.5	66	18.8
	18.5-24.9	225	63.9
	≥25	61	17.3
WHO clinical stage	Non advanced	115	32.7
	Advanced	237	67.3
CD4 count	<200	134	38.1
	≥200	218	61.9
Tenofovir-based regimen	No	100	28.4
	Yes	252	71.6

Serum creatinine estimated by chronic kidney disease epidemiology collaboration method indicated that 73(20.7%) of the study participants on ART patients had estimated GFR below 60 ml/min/1.73 m^2. Therefore the prevalence of renal function impairment was 20.7 %.(**Figure 3**)

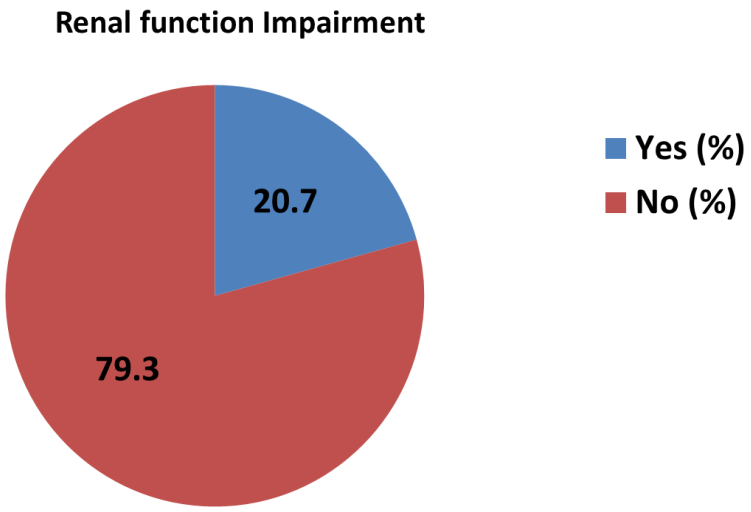

Figure 3. The prevalence of renal function impairment of HIV patients on ART attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest Ethiopia, 2020

5.4. Factors associated with renal function impairment among adult HIV positive individuals

5.4.1. Bivariable analysis

In bivariable logistic regression ten variables including sex of the participants, age of the participants, smoking cigarette, presence of comorbidity, having diabetes mellitus, having hypertension, tenofovir based regimen, less than 18.5 body mass index, advanced world health organization clinical stage and low CD4 count showed association with renal function impairment at P-value ≤ 0.25 **(Table 4)**.

Table 4: Bivariable analysis of factors associated with renal function impairment among HIV patients attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest Ethiopia, 2020

Characteristics	Categories	Renal function impairment		Crude OR (95% CI)	P-value
		No(n=279)	Yes(n=73)		
Sex	Male	117	37	1	
	Female	162	36	0.70[0.42-1.18]	0.181*
Age	<40	139	40	1	
	≥40	140	33	0.82[0.49-1.37]	0.050*
Marital status	Single	58	12	1	
	Married	163	44	1.31[0.65-2.64]	0.460
	Divorced	58	17	1.42[0.62-3.23]	0.410
Residence	Urban	220	54	0.76[0.76-1.38]	0.372
	Rural	59	19	1	
Educational status	No formal education	46	13	1.14[0.55-2.36]	0.725
	Primary education	31	15	1.95[0.94-4.04]	0.375
	Secondary education	73	13	0.72[0.35-1.45]	0.357
	Diploma and above	129	32	1	
Family history of renal impairment	No	255	68	1	
	Yes	24	5	0.78[0.29-2.12]	0.628
Occupation	Unemployed	59	27	3.07[0.64-5.74]	0.462
	Government employee	161	24	1	
	Self employed	33	10	2.03[0.89-4.65]	0.934
	Student	15	8	1.01[0.28-3.65]	0.992
	Other	6	9	10.06[0.45-30.79]	0.845
Income	<3500	127	48	0.65[0.35-3.47]	0.681
	≥3500	152	25	1	
cigarette Smoking	No	253	39	1	
	Yes	26	34	9.60[4.73-19.48]	0.000*
Comorbidity	No	221	35	1	

	Yes	58	38	4.14[2.40-7.12]	0.000*
Opportunistic infections	No	224	59	1	
	Yes	55	14	0.97[0.50-1.86]	0.918
Diabetes mellitus	No	252	50	1	
	Yes	27	23	6.16[2.79-13.59]	0.000*
Hypertension	No	251	59	1	
	Yes	28	14	4.71[1.98-11.17]	0.035*
Body mass index	<18.5	46	20	1.84[0.99-3.43]	0.054*
	18.5-24.9	182	43	1	
	≥25	51	10	0.83[0.39-1.77]	0.630
WHO clinical stage	Non advanced	101	14	1	
	Advanced	178	59	2.39[1.27-4.49]	0.007*
CD4 count	<200	86	48	6.47[3.31-12.64]	0.000*
	≥200	193	25	1	
Tenofovir-based regimen	No	73	27	1	
	Yes	206	46	0.60[0.35-1.04]	0.070*

OR, Odds Ratio; * statistically significant at P -value < 0.25, Other_ daily labor

5.4.2. Multivariable analysis

After controlling for possible confounder smoking cigarette, diabetes mellitus, hypertension and low CD4 count were statistically significantly associated with renal function impairment at p value less than 0.05.

Adult HIV positive individuals who are smoking cigarette were eight times [AOR= 8.48, 95% CI: 4.60-15.64] more likely to have renal function impairment as compared with an adult who did not smoke cigarette. Being hypertensive patient for adult on ART were two times [AOR= 2.13, 95% CI: 1.06-4.29] more likely to increase the risk of renal function impairment as compared to their counterpart, not hypertensive patient. Having diabetes mellitus increases the renal function impairment four times more likely for HIV positive adults [AOR= 4.29, 95% CI: 2.28-8.09] as compared with HIV positive individuals without diabetes mellitus. Furthermore, having low CD4 count for adult on ART were four times [AOR=4.31, 95% CI: 2.49-7.44] more likely to increase renal function impairment as compared with ART follower with high CD4 counts **(Table 5)**.

Table 5: Multivariable analysis of factors associated with renal function impairment among HIV patients attending ART clinics in Mettu Karl Referral hospital, Mettu town, southwest, Ethiopia, 2020.

Characteristics	Categories	eGFR (ml/min/1.73 m^2)		AOR(95% CI)	P-value
		≥60 N (%)	<60 N (%)		
cigarette Smoking	No	253(90.7)	39(53.4)	1	
	Yes	26(9.3)	34(46.6)	8.48[4.60-15.64]	0.001*
Diabetes mellitus	No	252(90.3)	50(68.5)	1	
	Yes	27(9.7)	23(31.5)	4.29[2.28-8.09]	0.001*
Hypertension	No	251(90)	59(80.8)	1	
	Yes	28(10)	14(19.2)	2.13[1.06-4.29]	0.001*
CD4 count	<200	86(30.8)	48(65.8)	4.31[2.49-7.44]	0.001*
	≥200	193(69.2)	25(34.2)	1	

* Statistically significant at P-value < 0.05

6. DISCUSSION

Renal impairment is a common sequel of HIV infection and it can be due to antiretroviral drugs or drugs used to treat certain opportunistic infections. Renal impairment, based on single creatinine clearance measurement, was very common among HIV infected adults with clinically non advanced HIV disease in most part of Africa (61).

The prevalence of renal function impairment in this study based on glomerular filtration rate using the CKD EPI estimation equation was 20.7%. This finding is consistent with the other similar studies done in southwest Nigeria (23.7%), in South Nigeria (24.3%), in Gondar (16.3%) (48,49,57). But it is higher than that studies which reported 14.5% in Ghana, 12.9% in Felege Hiwot referral hospital, Northwest Ethiopia and 7.6% in Jimma University Specialized hospital, Southwest Ethiopia (15,16,51). This variation may be due to the difference in among studies included in this study, the study in Ghana did not include hypertensive and diabetic individuals and whereas cigarette smokers did not include in the study from Northwest Ethiopia and Southwest Ethiopia. In addition, the method used to estimate GFR was also different; modified diet of renal disease formula was used to estimate GFR in Ghana, Cockcroft-Gault method in northwest Ethiopia and southwest Ethiopia which might also contribute to the variation in the prevalence.

However, the prevalence of renal function impairment in this study is lower than studies from Cote d'Ivoire (26%), Burundi (45.7%) Tanzania (25%) and Addis Ababa (25.4%) (24,26,55,62). This difference could be in part due to differences in ART regimen, study design, populations studied, stage of HIV infection and the sample size may contribute to the differences observed.

This study found that having hypertension heightened the risk of renal function impairment. This finding is concordant with those studies conducted in Brazil (17), Washington (63), London (64) , and Turkey (65). This might be due to the incidence of serum creatinine increases among hypertensive patients as compared to patients with normal blood pressure (66). In addition, it may be because kidney is one of the principal target organs of hypertension and most disease of kidney is associated with blood pressure elevation.

The current study also found that having diabetes increased the risk of renal function impairment. This finding is in agreement with previous similar studies done in middle income

countries (67), Sandi ago (68) and southern Ethiopia (59). The reason could be due to the fact that the common complication of diabetic called diabetic nephropathy decreases glomerular filtrations rate.

This study shows that those patients with low CD4 count were found to be more likely to develop renal function impairment. This is consistent with previous studies done in northwest Ethiopia (15) and southwest Ethiopia (16). The possible reason might be immunological AIDS (CD4 count <200 cell/μl) is known to be associated with development of opportunistic infections, malignancies and other organ diseases that affects kidney functions.

In this study, cigarette smoking was positively associated with renal function impairment. This finding is in agreement with previous studies done in Japan (69) and France (70). The possible explanation as to how smoking leads to renal function impairment could be that vasodilator compounds such as nitric oxide and atrial natriuretic peptide repeatedly released after each cigarette smoked eventually cause chronic glomerular hyper filtration (71). GFR is therefore decreased during smoking, and this was accompanied by a significant decrease of filtration fraction and an increase in Reno vascular resistance (72).

Different studies found out that old age is an independent predictor for renal function impairment (16, 66, 73-75). The current study however couldn't show a consistent result. This variation may be due to the population variation and different age classification methods used.

This study found out that gender was not statistically significantly associated with renal impairment. This finding is not in line with the studies conducted in Gondar (58) and Jimma(16) that revealed being female is the main predictor of renal function impairment. The discrepancy could be explained by differences in sociocultural variability, difference in sample size, and population variation.

Strength and limitation of the study

Laboratory blood meal is done for each patient eGFR (ml/min/1.73 m^2

Limitations

The limitation of this study was: first of all, creatinine was measured at a single point in time; therefore, it may have included short term, reversible causes of renal impairment which may overestimate renal impairment. Secondly, there was no assessment for proteinuria. Thirdly, this

study has limitation by being cross sectional design, and the underlying causes of renal impairment were unknown with this study design.

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

Notably, this study reveals a high prevalence of renal function impairment among HIV positive adult ART clinic in Mettu Karl referral hospital. Regarding factors associated with renal function interventions to improve the renal function status of HIV positive adults should focus on improving the context in which HIV positive live, including improvement high CD4 count, manage hypertension, manage diabetes mellitus and stop cigarette smoking.

7.2. Recommendations

Based on the findings from this study the following recommendations are forwarded.

For health care service providers

- Encourage patients to check their blood pressure status each time they arrive at the hospital.
- Should counsel to stop on modifiable risk factor like smoking cigarette.
- Closely monitoring renal function of patients presented with history of diabetic patients to prevent complication related to renal function impairment.
- Closely monitoring renal function of patients presented with low CD4 count.

For Mettu Karl referral hospital

- Screening for renal function impairment among HIV patients on ART having factors identified in this study.

For Minister of Health

- Shall be prepared guideline which monitoring creatinine closely. The renal function test for HIV patients not as need it must be with a fixed interval since renal function impairment was high in HIV positive adults on antiretroviral therapy.

For researcher

- It shall be considered cohort study design with a large sample size to determine renal function impairment.

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ANNEXES

JIMMA UNIVERSITY

Institute of Health

Department of Epidemiology

Annex I: information sheet (English version)

Greeting My Name is _____; I am working in _____. I am a research team member of Jimma University; Department of Epidemiology. I would like to inform you that I would have a short interview concerning a study which is conducted for the partial fulfillment of master's in masters of public health in epidemiology. Before we go to our discussion, I will ask you to listen carefully to what I am going to tell you about the purpose and general condition of the study and tell me whether you agree or disagree to participate in this study.

The objective of this study is to assess the magnitude of Renal function impairment among patients attending ART clinic. You are invited to be one of the participants we will stay together for 10-15 minutes. The study will be conducted through interview, medical record review and 5ml of blood will be taken from your venous blood by laboratory technician there will be little pain us usual and urine specimen will be collected, i will inform you the result. The information you give us is confidential and will be used only for the study purpose. A code number will identify every participant. Only summarized information of the total participant will be disseminated. The interview is voluntarily and you have the right to stop at any point of the interview. Your refusal will not have any effect on services that you get from the Hospital. However, your participation is important to fulfill the study.

Are you willing to participate in the study? 1. Yes 2. No

Thank you! (If the participant agrees to participate start interviewing if not say good bye).

Annex II: Informed consent form

I understand all the information provided to me by the data collector, the research conducted in our follow up hospital requires my participation. I am willing to participate in the interview, provided that no information regarding me is transferred to the third parity. I also understand that the nature of the study is maintaining confidentiality and privacy and my willingness is considered and my right I can stop at any point if there is any inconvenience. Therefor I am willing to participate in the study.

Signature ---------- Date ----------

Data collector name_____ signature_____

Annex III: English version questionnaires

Part-I: Socio-demographic characteristics			
S. No	Questions	Responses Options	
101	Respondent sex	1. Male 2. Female	
102	Age (In completed year)	_____	
104	Marital status	1. single 2. married 3. Divorced 4. widowed	
105	Educational status (encircle only the highest grade completed)	5. No formal education 6. Only read and write 7. 1-4 grade 8. 5-8 grade 9. 9-12 grade 10. Diploma and above	
105	Ethnicity	1. Oromo 2. Amhara 3. Others (specify)_____	
106	Religion	1. Muslim 2. Orthodox 3. Protestant 4. Catholic 5. Others (specify)_____	
107	Occupation	1. Unemployed 2. Government employee 3. Self-employed 4. Student 5. Others	
108	Residence location	1. Urban 2. Rural	
109	Household monthly income (in Birr)	_____	
110	Family history of renal disease	1. No 2. Yes	
Part-II: behavioral factors			
201	Have you ever smoked cigarette?	3. No 4. Yes	If No Skip to Q301

202	If Yes to Q201 how is the frequency	1. Monthly 2. Weekly 3. Once or twice weekly	
203	Do you currently smoke Cigarette?	1. No 2. Yes	If No, skip to Q301
204	If yes to Q203 how is the frequency you used?	1. Monthly 2. Weekly 3. Once or twice weekly 4. Daily/almost daily	

Part-III: HIV-related/bio-clinical factors			
S. No	Questions	Response	
301	Baseline CD4 cell count	_____ (cell/µl)	
303	Weight	_____(Kg)	
304	Height	_____(M)	
305	Body mass index	_____(Kg/m^2)	
306	serum creatinine		
307	*eGFR*		
308	Baseline WHO clinical stage	1. Stage-I 2. Stage-II 3. Stage-III 4. Stage-IV	
310	ART interruption history	1. No 2. Yes	
311	Presence of opportunistic infections	1. No 2. Yes	
313	Presence of comorbidity	1. Diabetes Yes no 2. Hypertension Yes no	

314	Current ART regimen	1. 1st line regimen 2. 2nd line regimen 3. 3rd line regimen	
315	Tenofovir-based regimen	1. No 2. Yes	
316	ART Doses given per day	1. Once a day 2. Twice a day 3. Three times a day	
317	Functional status	1. Working 2. Ambulatory	

THANK YOU! I have finished my interview.

Annex IV: Oddeeffaannoo

Duraan dursee nagaa isin gaafachaa, Ani maqaan koo :_____ kanan hojjechaa jiru:_____ . Ani yuunivarsiitii Jimmaatti miseensa garee qo'annoo damee barnoota Epiidiimooloojiitii. Kanan isinitti himuu barbaadu Aaf-gaaffii yeroo gabaabaa xumuura barnoota digirii 2ffaa muummee fayyaa hawaasaatti damee barnoota Eppiidiimooloojiidhaafi. Utuu gara mariitti hin darbiin, waa'ee dhimma isinitti himuuf barbaadu namusaan akka na dhaggeeffattaniif faayidaa fi haala qo'annoo irratti walii galuu fi waliigaluu dhiisuun irratti hirmaadhaa.

Kaayyoon qo'annoo kana namoota kiliniika ART hospitaala keenyaatti fayyadaman keessaa hammam isaanii Kaleen isaanii haalaan akka hojjechaa hin jirre adda baasuufii. Isinis akka hirmaataa tokkotti waan filatamtaniif daqiiqaa 10-15 nu waliin turtuu.

Qo'annoon kun kan gaggeeffamu maloota armaan gadii fayyadamuun ta'aa:

i. Aaf-gaaffii taasisuun
ii. Galmee yaalumsaa sakatta'uun
iii. Saamuda dhiigaa 5ml hidda dhiigaa irraa ogeeyyii teekiniishaana laaboraatootiin fuuchuun (Hub. Dhiigni yommuu fuudhamu akkuma yeroo kaanii dhukkubbiin salphaa ta'ee bakka lilmeen waraanutti dhaga'amuu danda'aa).

Iccitiin odeeffannoo isin nuuf kennitanii kan eegamuuf qo'annoo kana qofaaf kan oolu ta'aa. Hirmaataan hundi koodii dhuunfaan kan adda ba'uu ta'aa. Xumuura qo'annoo irratti cuunfaan argannoo qofti kan ifoomu ta'a.

Aaf-gaaffiin kun fedhii keessan irratti kan hundaa'eef qabxii barbaaddan irratti dhaabuuf mirga qabduu. Aaf-gaaffii kana yoo diddan tajaajila isin hoospitaala kana irraa argattan irratti dhiibbaa kamiyyuu kan hin qabne ta'uus hirmaannaan keessan garuu qo'annoo kana xumuuruuf baayyee murteessaadhaa.

Galatoomaa!

Annex V: Afan oromo version questionnaires

S.NO	Gaaffii	Filannoo deebi	
101	Saala	1,dhiira 2,dhalaa	
102	Umurii (waggaadhan)	_____	
103	Sadarkaa barnoota	1.kan hin baranne 2. dubbisuu fi barreessuu kan danda'u 3.kutaa 1-4 4.kutaa 5-8 5.kutaa 9-12 6.diploomaa fi isaa ol	
104	Saba	1.Oromoo 2.Amhara 3. kan biiro(adda baasi)_____	
105	Amantii	1.Musilima 2.Ortodooksii 3.Piroteestaantii 4.Kaatolikiii 5. kan biiro(adda baasi)_____	
106	Gahee hojii	1.Hojii dhabaa 2.Hojjetaa mootummaa 3.Hojjataa dhuunfaa 4. Barataa 5. kan biiro(adda baasi)_____	
107	Bakka Jireenyaa	1.Magaala	

		2.Baadiyyaa	
108	Galii ji'aan argamu(qarshiidhan)	_____	
109	Maati keessaa dhukkuba kalee kan qabu jiraa?	1.Eeyyee 2.Lakki	
Kutaa II Agarsiistuu Amala			
201	Kanaan Dura Tamboo Xuuxxee Beektaa?	1.Lakki 2. Eeyyee	
202	Yoo gaaffii 201 eeyyee tahe hagamiif	1.ji'aan 2.torbee 3. torbeetti al tokko ykn al lama	
203	Yeroo ammaa kana tamboo xuuxaa jirtaa?	1.Lakki 2. Eeyyee	
204	Yoo gaaffiin 203 eeyyen tahe hammam fayyadamta	1.ji'aan 2.torbee 3. torbeetti al tokko ykn al lama 4. Guyyaa hunda	